Internal Medicine Clerkship
Case Discussions

Acute Kidney Injury
Faculty Answer Guide

Objectives:

1. Identify characteristics and relevant review of systems that may indicate a specific etiology of acute kidney injury including fevers and arthralgia.
2. Assess past medical history for risk factors and predisposing conditions including causative medications and toxin exposures.
3. Identify key physical exam findings that assess volume status (including orthostatic blood pressure measurement, jugular venous pressure, and presence of edema) and assess presence of uremic symptoms (including pericardial rub and asterixis).
4. Identify and interpret key laboratory and imaging tests and list indications, benefits, test characteristics, risks, and costs of testing:
    a. Identify presence of acute kidney injury including patients with rising serum creatinine or decrease urine output.
    b. Determine underlying etiology including urinalysis with microscopic evaluation, urine chemistries, chemistry panel, and renal ultrasound.
5. Develop and prioritize a differential diagnosis including common and non-to-miss diagnoses:
    a. Distinguish pre-renal, intra-renal, and post-renal causes:
        i. Describe pre-renal causes including ineffective circulating volume.
        ii. Describe intra-renal causes including glomerular, tubular, interstitial, and vascular etiologies.
        iii. Describe post-renal causes including ureteral obstruction and bladder outlet obstruction.
6. Describe a rational and evidence-based approach to treating a patient with acute kidney injury:
    a. Describe treatment of acute conditions including hyperkalemia and fluid deficit.
    b. Describe treatment based on etiology including relieving obstruction in bladder outlet obstruction and withdrawal of causative medications in active interstitial nephritis.
7. Describe the long-term renal prognosis for patients with acute kidney injury.
8. List clinical interventions that may prevent acute kidney injury in patients at increased risk including discontinuation of causative medications, prevention of hypotension, and judicious use of iodinated contrast.

Clinical Case 1:

A 26-year-old male was admitted to the hospital complaining of generalized muscle soreness. He had completed the Boston Marathon three days prior to admission. He has become progressively anorexic and lethargic. He also noticed a decreasing amount of urine output over the past three days.

Medical history: Unremarkable and he was not taking any prescription or over the counter medication. He denied alcohol and illicit drug use.

Allergies: None known

Family history: Unremarkable for renal disease.

Physical Exam:
Well-developed, well-nourished male appearing lethargic
BP 135/70, pulse 84, respirations 20, temp afebrile, weight 80 kg
HEENT was unremarkable
Cardiac – S1, S2 without S3, S4, murmur or rub
Pulmonary – clear to auscultation and percussion
Abdomen – Supple and non-tender
Extremities – both lower extremities were tender and had 2+ edema
Neuro – no focal deficits. He was oriented to person, place and time, but was somnolent and had difficulty performing simple mathematical calculations.

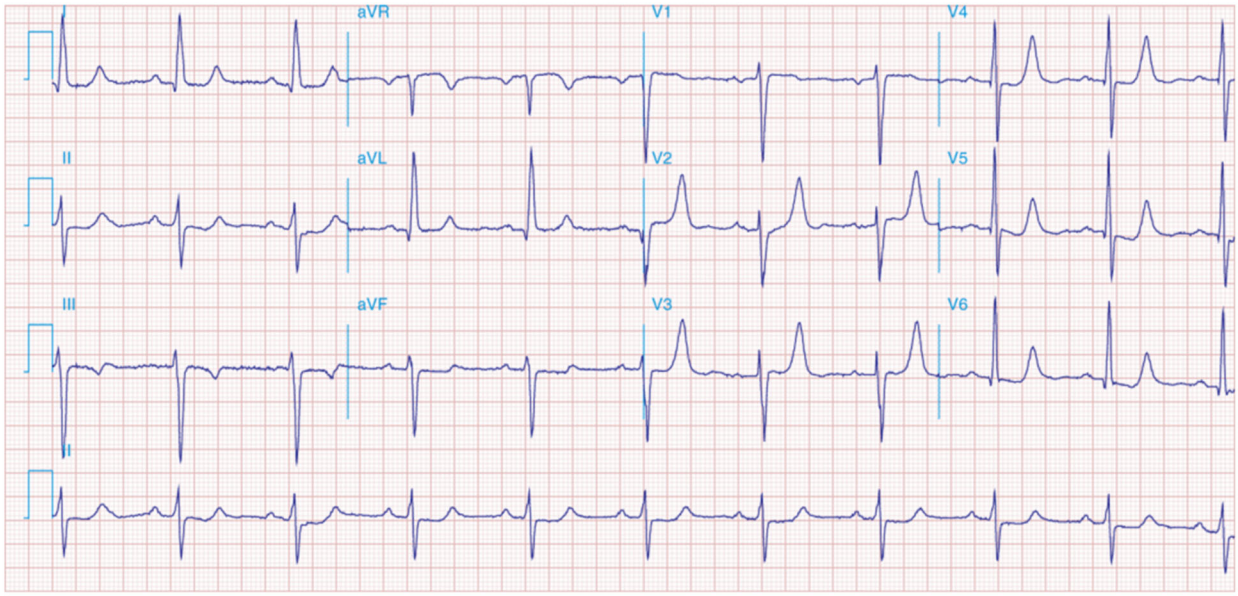
Laboratory Data:
Sodium 138 meq/L
Potassium 7.0 meq/L
Chloride 101 meq/L
Total C02 15
BUN 150 mg/dl
Creatinine 10 mg/dl
Glucose 100 mg/dl
Calcium 7.0 mg/dl
Phosphorus 8.0 mg/dl
Albumin 3.5 g/dl

Arterial Blood Gas: pH 7.35/28/105/15

Urine:
Specific gravity 1.015, pH 6.0, protein 2+, blood 4+, ketones (negative), glucose (negative) 2-5 RBC/HPF, 0-2 WBC/HPF
Na 35 meq/L, creatinine 56 mg/dl
UOSM 320.

Renal ultrasound – right kidney 10.8 cm, left kidney 11.0 cm. Normal echogenicity without calculi or hydronephrosis.

EKG is below:



Questions:

1. 1.Interpret the EKG above. What accounts for the changes noted? What other findings on EKG are often seen in a patient with severe acute kidney injury?

   Sinus rhythm with left ventricular hypertrophy, possible left atrial enlargement, inferolateral ST depressions (II, III, avF and V6), left anterior fascicular block, and slightly prolonged QT interval.

   EKG abnormalities seen with hyperkalemia range from peaked T waves with sinus rhythm to absence of the p wave with marked prolongation of the QRS complex which merges with the T wave forming the classic sine-wave pattern that is frequently misdiagnosed as ventricular tachycardia; the prolonged QT is often secondary to associated hypocalcemia. The sine-wave pattern is seen with more severe elevations of the potassium level (K+ > 8meq/l). The electrocardiogram may further degenerate to ventricular fibrillation or asystole. In addition to this classic sequence of events outlined above, virtually any type of arrhythmia or conduction disturbance may occur.

2. What are the three broad categories acute kidney injury can be divided into?

   Acute kidney injury can be divided into prerenal azotemia, intrinsic renal parenchymal disease, and postrenal obstruction. These are differentiated by clinical findings and laboratory data, specifically renal ultrasound, urinalysis, and urine electrolytes.

3. Utilizing the urine and blood chemistry values, how can one distinguish between prerenal azotemia and intrinsic renal disease? Calculate the fractional excretion of sodium.

   Prerenal acute kidney injury can be distinguished from intrinsic renal disease by the fractional excretion of sodium. A FENA of >1% is consistent with intrinsic disease. A fractional excretion of sodium <1% is seen in patients with prerenal causes of renal failure. The fractional excretion of sodium is calculated by (Urine Na x Plasma cr) / (Urine cr x Plasma Na) x 100. In this case 4.5%.

   The fractional reabsorption of water can also be used to distinguish these two types of acute renal failure. This is calculated by (100 – (100/UCR/SCR). A value of <97.5 is consistent with acute tubular necrosis. In this case (100 – (100/5.6) = 82%.

   Urine to serum creatinine ratio will be <20 in cases of intrinsic disease and >40 in patients with a prerenal cause of acute renal failure. In this case 56/10 = 5.6.

4. Based on the information provided, what is the most likely etiology of the patient's renal failure? What additional tests would be helpful in confirming the diagnosis?

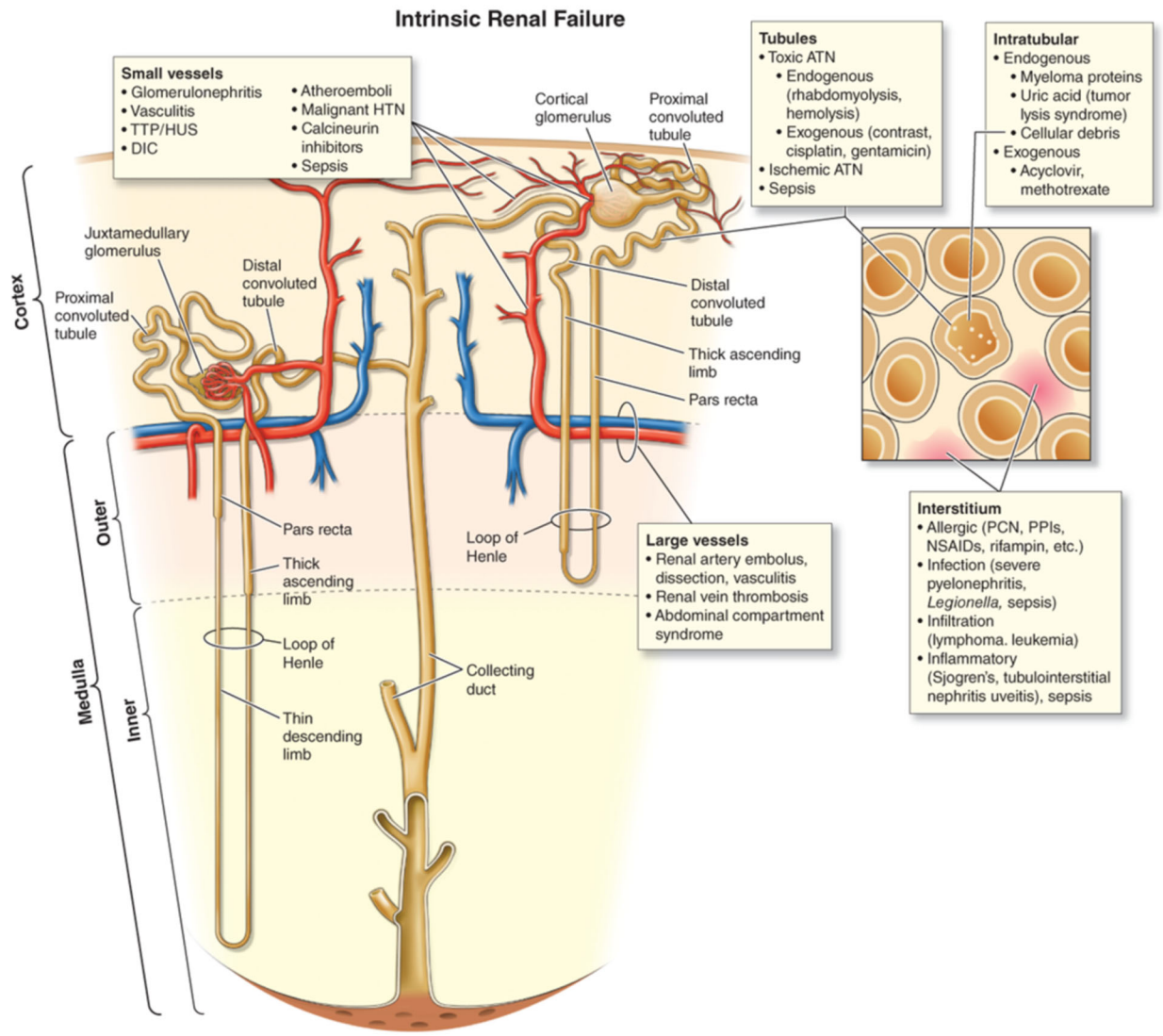
   This patient most likely has intrinsic renal disease, likely acute tubular necrosis specifically, secondary to rhabdomyolysis. The recent history of running in a marathon along with the presence of acute renal failure associated with 4+ blood on dipstick and 2-5 RBCs is consistent with the presence of myoglobinuria.

   Additional tests that would be useful are CPK and urine myoglobin.

5. In addition to the patient’s clinical condition, what are other common causes of acute intrinsic kidney failure?

   The most common causes of intrinsic acute kidney injury are sepsis, ischemia, nephrotoxins, both endogenous and exogenous. Often prerenal azotemia progresses to tubular injury. This type of acute kidney injury is often called acute tubular necrosis though in general inflammation, apoptosis, and altered renal perfusion may be important contributors. ATN is often diagnosed clinically with biopsy in settings such as sepsis without biopsy but there may often be additional factors at play include drug-induced interstitial nephritis and immune complex glomerulonephritis.

   The below graphic nicely summarizes all the different causes of intrinsic renal failure:



Source: J.L. Jameson, A.S. Fauci, D.L. Kasper, S.L. Hauser, D.L. Longo, J. Loscalzo: Harrison's Principles of Internal Medicine, 20th Edition

6. How would you interpret the renal ultrasound findings in this case?

This ultrasound demonstrates a normal kidney by size and echogenicity. This is consistent with the presence of acute kidney injury and not chronic kidney disease. These patients tend to have a better chance of recovering normal renal function than a patient who has underlying renal disease, which would be manifested by increased echogenicity and small kidneys. This ultrasound also rules out the likelihood that obstruction is responsible for the acute kidney injury. It should be kept in mind that patients with renal obstruction might have low, normal, or increased amounts of urine output due to a solute diuresis and for this reason one cannot make the diagnosis of obstruction on the basis of urine volume. Anuria is most often seen in two conditions, complete bilateral urinary tract obstruction or severe shock leading to cortical necrosis.

7. What are the indications for dialysis in general?

   AEIOU

   Acidosis in a patient that is volume overloaded and unable to respond to diuretics. These patients benefit from the ultrafiltration associated with dialysis as well as the high bicarbonate level in the dialysate. If they are not volume overloaded the patient can be treated with bicarbonate supplementation.

   Electrolyte disturbances such as hyperkalemia, which is the most common indication to dialyze.

   Intoxication with substances that are dialyzable. In general, any drug which is not protein bound can be dialyzed.

   Overload – Fluid overload not responding to medical management and compromising respiratory status.

   Uremia is another indication for acute dialysis and is diagnosed by the presence of pruritus, confusion, lethargy, inability to concentrate, nausea and emesis. An elevated BUN in the absence of any of these clinical findings is not itself sufficient to require acute dialysis.

8. What are the indications for dialysis specifically in this patient?

   This patient exhibits signs of uremia and has EKG findings secondary to hyperkalemia.

9. How would you acutely manage the hyperkalemia in this patient?

   Several options are available to treat hyperkalemia:

   The administration of 10-20 ml of 10% calcium gluconate is recommended to stabilize the cardiac membranes and has an immediate onset of 1-3 minutes. The effects of this infusion last for ~30-60 minutes. If no response is seen in 5-10 minutes, a second dose can be administered. If the patient does not respond to the second dose, it is unlikely that additional calcium will be of any benefit.

   Increasing the serum bicarbonate concentration will shift potassium into the cells. However, the effect of this treatment is greatest when the patient has acidemia and a low ph. Sodium bicarbonate is administered intravenously as a 50 meq bolus over 5 to 10 minutes, and the effect lasts for ~ 2 hours.

   Intravenous insulin stimulates cellular potassium uptake. This is due to the direct effect of insulin on the cell membrane. Glucose is administered to prevent hypoglycemia. The usual dose is 10 units of insulin combined with 100 ml of 50% glucose solution. The onset of the insulin effect is usually 30 minutes and lasts for up to 4 hours.

It should be kept in mind that these are at best only temporizing measures and the potassium must be removed from the patient by dialysis or a cation-exchange resin such as kayexalate or patiromer or zirconium cyclosilicate. Kayexalate works in the GI tract by promoting the exchange of potassium for sodium along the gastrointestinal tract. Each gram of resin removes .5 to 1 meq of potassium in exchange for 2 to 3 meq of sodium. Significant amounts of calcium and magnesium also may be removed. Patiromer works similar to kayexalate but is a cation exchange polymer that contains a calcium-sorbitol counterion instead of sodium. Zirconium is an inorganic, non-absorbable crystalline compound that exchanges both sodium and hydrogen ions for potassium throughout its intestinal transit. These exchange resins should be avoided in the setting of acute abdomen or post major abdominal surgeries as there is a risk of intestinal ischemia especially with kayexalate.

10. This patient has hyperkalemia, hypocalcemia, and hyperphosphatemia. What factor(s) are responsible for these derangements?

    The hyperkalemia in this patient is due to the extensive muscle damage, which has occurred and resulted in the release of potassium from the intracellular stores. We have ~50 meq/kg body weight of potassium most of which is intracellular.

    The hypocalcemia is due to the muscle necrosis, which results in severe hyperphosphatemia. This is due to the release of phosphate compounds from the muscle and facilitates the deposition of calcium and phosphate in soft tissues. Widespread soft tissue calcification has been described shortly after the onset of renal failure in these patients.

    In addition, acute kidney injury itself will cause these abnormalities, though they are generally more severe in the setting of rhabdomyolysis.

Clinical Case 2:

74yo with hx of hypertension, diabetes, heart failure with reduced ejection fraction of 30%, and benign prostatic hypertrophy who is brought to the emergency room by his family with lethargy, decreased oral intake, and fever for two days. They note his temperature at home reached 101.0 F. His current medications include carvedilol 12.5mg BID, losartan 25mg daily, furosemide 40mg BID, metformin 1000mg BID, and tamsulosin 0.4mg daily. His family reports he has been compliant with these medications.

Physical Exam:
Older, frail appearing male
BP 101/58, pulse 98, respirations 20, temp 101.4F
HEENT notable for dry mucous membranes and poor dentition
Cardiac – borderline tachycardic, + S4 and 2/6 systolic murmur heard best at the RUSB
Pulmonary – clear to auscultation and percussion
Abdomen – Supple and non-tender
Extremities – venous stasis changes noted with trace LEE b/l
Neuro – drowsy but able to respond to questions. No focal deficits noted on exam

Laboratory Data:
Sodium 128 meq/L
Potassium 5.4 meq/L
Chloride 110 meq/L
Total C02 18
BUN 150 mg/dl
Creatinine 4.2 mg/dl (baseline 1.8)
Glucose 168 mg/dl
Calcium 8.2 mg/dl
Phosphorus 4.0 mg/dl
Albumin 3.7 g/dl

WBC 12.8 k/UL
Granulocyte 8.0 k/mm3
Hgb 11.6 gm/dl
Plt 450 k/UL

Urine:
Specific gravity 1.6, pH 5.8, protein 1+, blood 1+, ketones 2+, glucose (negative), 2-5 RBC/HPF, 10-20 WBC/HPF, + leukocyte esterase, + nitrates, + hyaline casts, 3+ bacteria
Na 20 meq/L, creatinine 100 mg/dl, urea 400mg/dl

Questions:

1. Based on the information provided, what is the most likely etiology of the patient's renal failure? Discuss FeNa versus FeUrea.

   This patient is borderline hypotensive and tachycardic, appears dry on exam, and has reported history of poor oral intake. In addition, he is having fevers which may increase his extraneous volume losses. His urinalysis would suggest a urinary tract infection as the cause of his symptoms. It is likely based on this information that he is experiencing prerenal azotemia.

   This can be further confirmed by calculating is FeNa which is 0.655%. However, this patient is on a diuretic which can increase sodium excretion into the urine and therefore falsely elevate the FeNa value.

   FeUrea is calculated as (Urine urea x Plasma cr) / (Urine cr x Plasma Urea) x 100.
   In this case if you calculate the FeUrea it is 11.2% which also suggests a prerenal etiology.

   In addition, the presence of hyaline casts in his urine is associated with a prerenal etiology.

2. How would you treat this patient? Would you make any changes to his medications?

   The key principle for management of prerenal azotemia is correct of fluid and electrolyte imbalances, discontinuation of nephrotoxic medications, and dose adjustment of any

critical medications. He should be treated with fluid replacement, although the rate of replacement should be monitored closely given his reduced ejection fraction. His metformin, losartan, and furosemide should all be temporarily held as these can worsen his kidney function or promote further volume loss. They should be restarted when his kidney function recovers significantly. His urine output should be monitored given his baseline BPH and risk for obstruction; a normal urine output is 0.5 to 1.5 cc/kg/hour. He should be initiated on medications to empirically treat his urinary tract infection, although a renal ultrasound can also be considered to evaluate for obstruction and assess for complications of an ascending infection (i.e. pyelonephritis) that may require a change in management.

3. What is this patient's prognosis for his acute kidney injury?

   The kidney has a remarkable capacity to repair itself even after severe acute injury, which would suggest with proper treatment this patient will likely fully recover. Patients who have acute kidney injury on superimposed chronic kidney disease may not recover fully and may be at higher risk for progression of their baseline disease or dialysis.

The patient is treated appropriately, his mental status improves, his fevers resolve, and his urine output increases. On day three of his hospital stay, the nurse notes that his urine output has started to decline again. His vitals have remained stable, a repeat urinalysis is negative, and his white blood cell count has normalized. His creatine improved from 4.2mg/dl to 2.0mg/dl but is now 2.3mg/dl.

4. What do you suspect is happening to the patient currently, and how would you evaluate him?

   It appears his urine infection is improving but his urine output has fallen off and his creatinine is on the rise again. At this point, you would be most concerned that the patient has developed symptomatic urinary obstruction that is now leading to a postrenal acute kidney injury. A post void residual and possibly a renal ultrasound to assess for location of obstruction should be obtained.

A post void residual is completed and shows a volume of 250mL. A renal ultrasound shows mild bilateral hydronephrosis.

5. How would you manage the patient at this point?

   A urinary catheter should be placed to help relieve the obstruction. If this promotes diuresis, then this is usually sufficient treatment. However, if his post void remains elevated urology should be consulted for further management.

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